multiple-step sections may be required to detect the worm.[14] It may also be appropriate to initiate a public health campaign directed toward the education of pet owners and the control of this disease in dogs, as suggested by Hansen.[10]

Summary

A 67-year-old man, under treatment for adenocarcinoma of the prostate since September 1978, was found to have a mild respiratory illness in January 1979. An x-ray study of the chest, which had shown no abnormalities in September 1978, now showed a *coin* lesion in the right lower lobe. When noninvasive techniques failed to clarify the nodule's cause, the affected lobe was excised. The nodule contained an adult male *Dirofilaria immitis*. Epidemiologic data indicate that the patient probably acquired the infection in Lake Combie, Placer County, California, in the summer of 1978. It is postulated that this event was the result of increasing prevalence of heartworm infection in an expanding canine population, high levels of mosquito densities in 1978 and the proper human exposure. Available data suggest that in some areas of the western states conditions are suitable for the transmission to humans of this zoonosis and, therefore, physicians are urged to include this possibility in the differential diagnosis of solitary pulmonary nodules.

REFERENCES

1. Dashiell GF: A case of dirofilariasis involving the lung. Am J Trop Med Hyg 10:37-38, Jan 1961

2. Otto GF: Changing geographic distribution of heartworm disease in the United States (pp 1-2); and Occurences of the heartworm in unusual locations and in unusual hosts (pp 6-13), *In* Morgan HC, et al (Eds): Proceedings of the Heartworm Symposium '74. Bonner Springs, Kansas, Veterinary Medicine Publishing Co., 1975

3. Annual Report of Local Rabies Control Activities. State of California, Department of Health Services, 1960-1976

4. California Statistical Abstract 1976. State of California, Documents Section, Table B-5, p 8

5. Otto GF: Epizootiology of canine heartworm disease. *In* Bradley RE (Ed): Canine Heartworm Disease: The Current Knowledge. Gainesville, FL, University of Florida, Dept Vet Sc, Inst Food Agr Sc, 1972, pp 1-15

6. McGreevy PB, Conrad RD, Bulgin MS, et al: Canine filariasis in Northern California. Am J Vet Res 31:1325-1328, Jul 1970

7. Wood G, quoted in American Heartworm Society Bull 5:4, Jul 1979

8. Weinmann CJ, Garcia R: Canine heartworm in California, with observations on *Aedes sierrensis* as a potential vector. Cal Vector Views 21:45-50, Aug 1974

9. Weinmann CJ, Garcia R: Coyotes and canine heartworm in California. J Wildlife Dis 16:217-221, Apr 1980

10. Hansen CP: The sudden rise of dog heartworm (*Dirofilaria immitis*) to a serious pest level in San Mateo County. Proc Cal Mosq Vect Cont Assoc 46:15-16, Jan-Feb 1978

11. Jackson R, quoted in American Heartworm Society Bull 5: 4, Jul 1979

12. Ludlam KW, Jachowski LA Jr, Otto GF: Potential vectors of *Dirofilaria immitis*. J Am Vet Med Assoc 157:1354-1359, Nov 1970

13. Reeves WC, Milby MM: Encephalitis viral activity and vector populations in California—Present and future concerns. Proc and Papers of the 47th Annual Conference of the Cal Mosq Vect Cont Assoc 47:1-6, Aug 1979

14. Harrison EG Jr, Thompson JH Jr: Dirofilariasis of human lung. Am J Clin Pathol 43:224-234, Mar 1965

Refer to: Murray BJ: Severe lactic acidosis and hypothermia. West J Med 134:162-166, Feb 1981

Severe Lactic Acidosis and Hypothermia

BRIAN J. MURRAY, MD, *San Diego*

SURVIVAL OF PERSONS with severe lactic acidosis and a pH of less than 6.9 is unusual. In general, mortality approaches 100 percent for patients with a pH of less than 6.9 or a lactate level of greater than 13 mEq per liter.[1-3] Although there are case reports of patients surviving with a pH of less than 6.9,[4-6] there are no cases reporting survival with a lactate level of greater than 20 mEq per liter and a pH as low as 6.67, as occurred in this patient. Survival was more probable in this woman because of concordant hypothermia. Hypothermia is known to decrease the metabolic rate and, consequently, allows a patient to tolerate better inactivation of vital intracellular enzymes during acidosis. The patient's clinical features were well correlated to the hypothermia.

Report of a Case

A 49-year-old woman was brought into the emergency room after she was found lying on the floor of her apartment semicomatose. She was able to give a limited history and complained of vague abdominal pains and two to three days of nausea and vomiting. She gave no history of loss of consciousness, diabetes mellitus, recent trauma or history of toxic ingestions. A review of hospital records disclosed that she had a history of chronic alcohol abuse, presumed alcoholic liver disease, folate-deficiency anemia, schizophrenia and dementia.

Physical Examination

In the emergency room her blood pressure was 88/60 mm of mercury while supine. Her pulse was 88 per minute and regular, respirations were 36 per minute and her temperature by rectal

From the Department of Medicine, Mercy Hospital and Medical Center, San Diego.

Submitted revised, May 13, 1980.

Reprint requests to: Brian J. Murray, MD, University of California, San Diego, Q-039, La Jolla, CA 92093.

probe thermocouple thermometer was 30.5°C (87.0°F). There was no evidence of a shivering reflex present.

The patient was lethargic with Kussmaul respirations. She was oriented to name and place. She had dry mucous membranes, and skin turgor was poor. Her weight was 66 kg (145.2 pounds). Blood pressure while sitting was not palpable or audible. There was no adenopathy and integument was unremarkable except for the noted hypothermia. The pupils were sluggish but equally reactive to light, and findings on funduscopic examination were normal. The neck was supple and there were no meningeal signs. The lungs were clear to auscultation and percussion. The pulses were decreased but present in all four extremities. Examination of the precordium disclosed a normal point of maximum impulse (PMI) and a grade 2 (on a scale of 6) systolic ejection murmur at the lower left sternal border. No rubs or gallops were noted. There was minimal tenderness of the abdomen over the upper quadrants. The liver was 10.0 cm by percussion and there were no masses or splenomegaly. Neurological examination showed garbled, slurred speech, and decreased gag and cough reflex. Cranial nerves II through XII were otherwise intact. The deep tendon reflexes were absent in the lower extremities and were symmetrically equal in the upper extremities with a delayed relaxation phase. The toes were down-going bilaterally and motor strength was felt to be equal in all four extremities. The remainder of the physical examination was unremarkable, except for the odor of alcohol on her breath.

Initial Laboratory Studies

Results of laboratory studies done in the emergency room were as follows: sodium 136, chloride 102, potassium 4.8 and bicarbonate 1.0 mEq per liter; blood urea nitrogen (BUN) 12, creatinine 1.0 and glucose 86 mg per dl; serum aspartate aminotransferase (SGOT; formerly known as serum glutamic-oxaloacetic transaminase) 235 IU per liter, serum alanine aminotransferase (SGPT; formerly known as serum glutamic-pyruvic transaminase) 38 IU per liter and amylase 562 IU per liter (normal less than 81); lipase 36 IU per dl (normal less than 24); phosphorus 6.5 mg per dl; osmolality 298 mOsm; leukocyte count 19,200 cells per cu mm, with a left shift, hemoglobin 14.5 grams per dl and mean corpuscular volume (MCV) 117. Analysis of urine showed proteinuria (4+), ketonuria (2+) and microscopic hematuria. Arterial blood gas studies obtained on room air and corrected for a core temperature of 30.5°C (87.0°F)[7] were as follows: oxygen pressure (Po_2) 91 mm of mercury and carbon dioxide pressure (Pco_2) 13 mm of mercury; bicarbonate 1.5 mEq per liter, and pH 6.67. The arterial blood gas measurements were rechecked and the results were confirmed. An electrocardiogram disclosed normal sinus rhythm and no acute changes. There was no ectopy and no J wave present. A roentgenogram of the chest showed a small superior segmental infiltrate of the right lower lobe, but no other abnormalities. After 100 mEq of sodium bicarbonate had been given parenterally and 1.5 liters of 5 percent dextrose and normal saline infused, a repeat arterial blood gas measurement corrected for a core temperature of 31.1°C (88.0°F)[7] showed a pH of 6.75.

Hospital Course and Treatment

A central venous pressure line was placed and measured 0 cm of water pressure. An arterial femoral line showed a core blood pressure of 88/40 mm of mercury. A Swan-Ganz line was placed a few hours later while the patient was in the intensive care unit. A nasogastric tube detected heme-positive material but no active bleeding. A lumbar puncture yielded normal cerebrospinal fluid on microscopic examination.

The patient was treated vigorously with intravenous fluid replacement consisting of 5 percent dextrose with normal saline and plasmanate (approximately 10 liters in 24 hours). Thiamine was given parenterally. She was given 600 mEq of sodium bicarbonate in 24 hours (12 ampuls with 50 mEq of sodium bicarbonate per ampul). Broad-spectrum antibiotic drugs and 1 gram of methylprednisolone sodium succinate (Solu-Medrol) were administered for suspected Gram-negative sepsis; 500 μg of sodium levothyroxine (Synthroid) was given intravenously for suspected myxedematous coma. A heating blanket was used and the patient's temperature was monitored continuously by rectal probe thermometer. The core rectal temperature increased by approximately 0.6°C per hour until it reached 37.0°C (98.6°F) within 12 hours after admission. The pH was corrected more slowly to a pH of greater than 7.25 during the second 24 hours

with the use of 400 mEq of sodium bicarbonate (8 ampuls of sodium bicarbonate). The pH continued to increase, to a level of greater than 7.55 after 48 hours of admission. The hypovolemia and hypotension were corrected with vigorous fluid management which included maximizing the wedge pressure and cardiac output. At no time was the patient oliguric. After hydration the hemoglobin diluted from 14.5 to 11.7 grams per dl. The patient's weight increased from 66 to 71.7 kg.

The elevated anion gap resolved within 72 hours. The studies of the elevated anion gap showed an arterial blood level of lactate to be 180 mg per dl, and pyruvate to be 0.5 mg per dl. Methanol, paraldehyde, ethylene glycol and salicylate levels were all negative. Serum ketones were positive at 1:4 dilution and serum osmolality was 298 mOsm. The alcohol level was 0.07 gram per dl. The lactate level decreased from 180 to 63 mg per dl within 24 hours of admission.

The random serum glucose level rose from 86 to 824 mg per dl within 24 hours of admission and ketones increased from 1:4 to 1:8 dilution. The diabetic ketoacidosis was managed with continuous infusion of low doses of insulin. The phosphorus level, which was originally 6.5 mg per dl (rechecked and confirmed) fell to less than 0.2 mg per dl after insulin infusion was begun for the hyperglycemic ketosis. This condition was successfully treated with potassium phosphate.

Serum amylase levels remained elevated and the amylase to creatinine clearance ratio obtained 24 hours after admission was greater than 10 percent. Intermittent nasogastric suctioning and intravenous hydration eventually led to resolution of the abdominal pain and return of amylase levels to normal.

Other causes for hypothermia that were ruled out included a coma panel which was negative for barbiturates and phenothiazines. Thyroid function studies obtained on admission showed a normal thyroid-stimulating hormone level (TSH) and a borderline normal free thyroxine index (T7). Pituitary and adrenal functions were deemed adequate on the basis of normal gonadotropin levels and a normal response to a metapyrone suppression test with appropriate elevation of 11-deoxycortisol (compound S).

Follow-up cultures of the blood, urine and cerebrospinal fluid (CSF) obtained on admission were all negative and antibiotic therapy was eventually discontinued. During the first few days after admission, there were evolutionary changes in the patient's EKG consistent with the diagnosis of subendocardial myocardial infarction; cardiac isoenzyme series for creatine phosphokinase (CPK) were also diagnostic for a myocardial infarction. However, the patient tolerated this infarction without any complications. The patient was discharged on the 15th hospital day in her usual state of health, euthermic, with a normal amylase and serum glucose levels. A repeat roentgenogram of the chest showed resolution of the previously noted infiltrate.

Discussion

The patient was admitted to hospital with a severe metabolic acidosis involving an anion gap of greater than 30. The severity of the acidosis and the subsequent survival of this patient are unique—to my knowledge there are no other such cases reported in the literature. The patient's survival appears to be, in part, a result of concomitant hypothermia which had a protective effect by decreasing metabolic demands by approximately 40 percent.[8]

The differential diagnosis for metabolic acidosis with an elevated anion gap is well reviewed elsewhere.[9] Although the ketones were positive at 1:4 dilution in the blood, this was not elevated enough to explain the severity of the acidosis. The arterial lactate level of 180 mg per dl was significantly elevated (normal less than 15 mg per dl). This represented a lactate level of 20 mEq per liter with a pyruvate level of less than 0.1 mEq per liter.

The cause of the elevated lactic acidosis in this case could have been due to a combination of any of the following: hypotension and hypovolemia, alcoholism, pancreatitis, diabetes or hypothermia.[10,11] Lactic acidosis resulting from hypothermia is not common but has been noted. It is secondary to microcirculatory insufficiency coupled with the shivering reflex which produces lactic acid.[11]

The clinical features of hypothermia (core temperature of less than 35°C [95°F]) are multiple and have been recently reviewed by Reuler.[11] In this case the hypothermia was felt to be secondary to ethanol and environmental exposure. Hypothermia in the alcoholic population is not unusual.[11,12] The central nervous system depressant effects and the vasodilatory

effects coupled with environmental exposure are the common explanations for this phenomenon.

Typical physical findings of hypothermia include absence of shivering, sluggish pupils, delayed reflexes, decreased mentation, decreased cough reflex and hypotension as the hypothermia progresses.[11,12] My patient exhibited all of these findings. A decreased cough reflex and cold-induced bronchorrhea often lead to aspiration pneumonia, which may have been present in this patient as she had a common segmental lobe involvement for aspiration when supine.

The hypovolemia could be attributed to the three-day history of vomiting, but this should have generated some bicarbonate, and the degree of metabolic acidosis should not have been as severe. Another explanation for the hypovolemia is cold diuresis.[11,13] The normal hemoglobin on admission in this patient with documented folate-deficiency anemia was probably secondary to hemoconcentration and splenic contracture seen in hypothermia.[11] Gastric submucosal hemorrhage is also common in hypothermia and may have accounted for the heme-positive nasogastric aspirate and for a portion of the subsequent drop in hemoglobin.[11]

The diagnosis of pancreatitis was supported by the symptoms, physical findings and an elevated amylase to creatinine clearance ratio of greater than 10 percent.[14] The cause of pancreatitis may have been alcohol abuse, but this condition has also been reported with hypothermia.[15,16] Furthermore, diabetic ketoacidosis in conjunction with acute pancreatitis, secondary to accidental hypothermia, is recognized.[17] The mechanism for diabetes mellitus with hypothermia is secondary to inhibition of insulin release[18] and decreased effectiveness of insulin, along with the pancreatitis itself.[17] It should be noted that hyperamylasemia and an elevated amylase to creatinine clearance ratio is not specific for the diagnosis of pancreatitis in the presence of diabetic ketoacidosis.[14,19] However, with the ratio of greater than 10 percent, it is likely that the pancreas was the source of the elevated levels of serum amylase.

The possibility that hypothermia develops as a consequence of diabetic ketoacidosis has also been suggested.[4] However, in these cases severe hyperglycemic-ketotic, hyperosmolar states are described. In this patient, the initial serum glucose value of 86 mg per dl rules out this possibility. The diabetic ketoacidosis, which in fact ensued hours after admission, was partially induced by the generous amounts of parenteral glucose infused in a hypothermic state[20] in which peripheral utilization of glucose was reduced. The rising ketonemia after starting the infusion of low doses of insulin undoubtedly reflected an improved oxidative state and consequent metabolism of β-hydroxybutyrate.[21]

The elevated level of phosphorus noted on admission has previously been described in cases of severe lactic acidosis.[3] The precipitous drop of serum phosphorus to 0.2 mg per dl could be attributed to the treatment phase of diabetic ketoacidosis, but it has also recently been observed to occur as a complication of the rewarming phase in hypothermia.[22] The methods available for rewarming hypothermic patients are by peripheral warming techniques and by internal methods.[23] The patient in this case tolerated the slow rewarming by peripheral means without difficulty. There was no observed drop in core temperature using the peripheral warming technique as has sometimes been described.[23]

Summary

A case of severe lactic acidosis with hypothermia is described. Survival of a patient with this degree of lactic acidosis is unique and, undoubtedly, was secondary to decreased metabolic demands present in a state of hypothermia. The cause of the lactic acidosis may have been secondary to the hypothermia alone. The patient was felt to be hypothermic as a result of environmental exposure in conjunction with an alcoholic state. The hypothermia could account for the clinical course of this patient, which included coma, aspiration pneumonia, hypovolemia, gastric submucosa hemorrhage, pancreatitis, transient hyperglycemic ketosis and hypophosphatemia. Management of the patient's condition with bicarbonate, fluids and peripheral warming techniques is briefly discussed.

REFERENCES

1. Peretz DI, McGregor M, Dossetor JB: Lactic acidosis: A clinically significant aspect of shock. Canad Med Assoc J 90:673, 1964

2. Peretz DI, Scott HM, Duff J, et al: The significance of lactic-acidemia in the shock syndrome. Ann NY Acad Sci 119:1133-1139, 1965

3. Tranquada RE, Grant WJ, Peterson CR: Lactic acidosis. Arch Intern Med 117:192-202, 1966

4. Gale EAM, Tattersall RB: Hypothermia: A complication of diabetic ketoacidosis. Br Med J 2:1387-1389, 1978

5. Garella S, Dana CL, Chazan JA: Severity of metabolic acidosis as a determinant of bicarbonate requirements. N Engl J Med 289:121-126, 1973

6. Fulop M, Hoberman HD: Phenformin-associated metabolic acidosis. Diabetes 25:292-296, 1976

7. Kelman GR, Nunn JF: Nomograms for correction of blood PO_2, PCO_2, pH, and base excess for time and temperature. J Appl Physiol 21:1484-1490, 1966

8. Blair E: Clinical Hypothermia. New York, McGraw-Hill Co, 1964

9. Emmett M, Narins RG: Clinical use of the anion gap. Medicine 56:38-55, 1977

10. Oliva PG: Lactic acidosis. Am J Med 48:209-225, 1970

11. Reuler JB: Hypothermia: Pathophysiology, clinical settings, and management. Ann Intern Med 89:519-527, 1978

12. Weyman AE, Greenbaum DM, Grace WJ: Accidental hypothermia in an alcoholic population. Am J Med 56:13-21, 1974

13. Moyer JH, Morris G, DeBakey ME: Hypothermia: I. Effect on renal hemodynamics and on excretion of water and electrolytes in dog and man. Ann Surg 145:26-40, 1957

14. Levitt MD: Clinical use of amylase clearance and isoamylase measurements. Mayo Clin Proc 54:428-431, 1979

15. Duguid H, Simpson RG, Stowers JM: Accidental hypothermia. Lancet 2:1213-1219, 1961

16. Read AE, Emslie-Smith D, Gough KR, et al: Pancreatitis and accidental hypothermia. Lancet 2:1219-1221, 1961

17. MacLean D, Murison J, Griffiths PD: Acute pancreatitis and diabetic ketoacidosis in accidental hypothermia and hypothermic myxoedema. Br Med J 4:757-761, 1973

18. Currey DL, Curry KP: Hypothermia and insulin secretion. Endocrinology 87:750-755, 1970

19. Vinicor F, Lehrner LM, Karn RC, et al: Hyperamylasemia in diabetic ketoacidosis: Sources and significance. Ann Intern Med 91:200-204, 1979

20. Wynn V: Electrolyte disturbances associated with failure to metabolise glucose during hypothermia. Lancet 2:575-578, 1954

21. Kreisberg RA: Diabetic ketoacidosis: New concepts and trends in pathogenesis and treatment. Ann Intern Med 88:681-695, 1978

22. Levy LA: Severe hypophosphatemia as a complication of the treatment of hypothermia. Arch Intern Med 140:128-129, 1980

23. Myers RAM, Britten JS, Cowley RA: Hypothermia: Quantitative aspects of therapy. JACEP 8:523-527, 1979